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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/587,681

07/29/2006

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NBG-116

8469

48388 7590 10/19/2009
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EXAMINER

BOWERS, NATHAN ANDREW

ART UNIT

PAPER NUMBER

1797

MAIL DATE

DELIVERY MODE

10/19/2009

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/587,681	Applicant(s) VASSANELLI ET AL.	
	Examiner NATHAN A. BOWERS	Art Unit 1797	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 17 July 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 4-15 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 4-15 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 29 July 2006 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>072906</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election/Restrictions

1) Applicant's election with traverse of Group II, claims 4-15 in the reply filed on 17 July 2009 is acknowledged. The traversal is on the ground that a special technical feature – an array of individually driven/controllable microelectrodes – is claimed in each Group and is not anticipated by Lewis or the prior art. Applicant's arguments are not found persuasive because, regardless of the merits of Lewis, the Xu (US 20050112544) reference clearly discloses that the use of an array of individually addressable microelectrodes is known in the art. Therefore this structure cannot be considered as a special technical feature. See the 35 U.S.C. 102 rejections below for a more detailed examination of Xu.

The requirement is still deemed proper and is therefore made FINAL.

2) Claims 1-3 and 16-26 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected inventions, there being no allowable generic or linking claim. It is noted that Applicant has cancelled claims 1-3 and 16-26. Applicant timely traversed the restriction (election) requirement in the reply filed on 17 July 2009.

Claim Objections

3) Claim 14 is object to because of the following informalities: lines 3-6 are grammatically unclear and difficult to interpret. More specifically, the structural

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relationship of the claimed gate and source of the transistor is not clearly worded. The claim limitations set forth in the phrase "a gate of these electrodes being realized in n+ doped polysilicon and common to all devices in a row, word line, the drain of all devices in a column being connected together by using a metal contact plug and a metal line, the source of the transistor being connected..." are difficult to interpret due to the phrase's stilted grammatical structure.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4) Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is unclear whether Applicant intends for the claim limitation "means to electrically connect" to invoke 35 U.S.C. 112, sixth paragraph. If applicant wishes to have this claim limitation treated under 35 U.S.C. 112, sixth paragraph, Applicant is required to:

- (a) Amend the claim to include the phrase "means for" in accordance with these guidelines: the phrase "means for" must be modified by functional language and the phrase must not be modified by sufficient structure, material, or acts for performing the claimed function; or
- (b) Show that the claim limitation is written as a function to be performed and

the claim does not recite sufficient structure, material, or acts for performing the claimed function which would preclude application of 35 U.S.C. 112, sixth paragraph. For more information, see MPEP 2181.

If claim element "means to electrically connect" is determined to be a means plus function limitations that invoke 35 U.S.C. 112, sixth paragraph, then it is understood that the written description does disclose the corresponding structure, material, or acts for the claimed function. Paragraph [0038] of Applicant's specification states that conductive traces and conductive pads are used to electrically connect the array of microelectrodes to external devices such as a switching system. Equivalent "means to electrically connect" would include any conductive wire or trace capable of connecting an electrode array to a switching system.

5) Claim 2 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "a couple" in claim 2 is a relative term which renders the claim indefinite. The term "a couple" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. The term "a couple" could be defined as meaning strictly "two," or informally could be defined as meaning "a few" or "several" which potentially could be different than "two." Accordingly, those of

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ordinary skill in the art would reach different opinions in determining how many external parallel connectors are required by claim 2.

6) Claims 12 and 14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "consisting of" in claims 12 and 14 is closed ended and excludes any element, step, or ingredient not specified in the claim. The term "consisting of" implies that the biochip is constructed only from the elements recited in claims 12 and 14.

Accordingly, claims 12 and 14 conflict with independent claim 4 which indicates that the biochip includes a cell culture chamber. The "consisting of" language of claims 12 and 14 would serve to exclude the cell culture chamber, as well as any other limitation set forth in claim 4 that is not expressly recited in claims 12 and 14. Applicant is encouraged to substitute the open term "comprising" for the closed term "consisting of." See MPEP 2111.03.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States

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only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

7) Claims 4, 5 and 7-11 are rejected under 35 U.S.C. 102(e) as being anticipated by Xu (US 20050112544).

With respect to claim 4, Xu discloses a biochip comprising an array of microelectrodes (Figure 1A:110, 120). Paragraph [0038] indicates that each microelectrode is positioned on a solid substrate. Paragraph [0048] further states that an insulating layer (i.e. silicone-dioxide) is provided on the substrate to form a strip upon which each microelectrode is positioned. Xu additionally teaches in paragraphs [0192] and [0198] that each microelectrode within the array is individually addressed and in communication with a switching system using conductive traces (Figure 1A:130) and conductive pads (Figure 1A:150). Paragraphs [0038] and [0040] teach that each microelectrode array is located at the bottom of a cell culture chamber formed by an individual well of a multi-well plate. Accordingly, cells can be grown and adhere in contact with the array of microelectrodes on a surface formed by the insulating layer of the solid substrate.

With respect to claims 5 and 9, Xu discloses the biochip set forth in claim 4. Additionally, Xu teaches that the substrate serves as a solid support upon which cell culture chambers and microelectrode arrays are formed. See paragraph [0038]. Paragraph [0048] indicates that the substrate is manufactured using dielectric materials such as glass or ceramics. Paragraph [0038] further describes the use of conductive traces (Figure 1A:130) and pads (Figure 1A:150) used to connect each microelectrode to external parallel connectors using wire bonding. Figures 13 and 14 describe how

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each microelectrode array is in communication with an external printed circuit board or electronic conductor lines capable of communicating with a switching system and/or an analysis device.

With respect to claim 7, Xu discloses the biochip set forth in claim 5. Furthermore, Xu teaches in paragraphs [0028] and [0048] that the substrate is manufactured from silicon, and that the insulating layer is silicone-dioxide.

With respect to claim 8, Xu discloses the biochip set forth in claim 5. Xu additionally teaches in paragraph [0181] that the substrate is formed using an optically transparent material.

With respect to claim 10, Xu discloses the biochip set forth in claim 5. Xu teaches in paragraph [0147] that each microelectrode may be 1 or 5 microns in width.

With respect to claim 11, Xu discloses the biochip set forth in claim 4. Xu further discloses in paragraph [0038] that the microelectrodes are constructed from electrically conductive materials.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8) Claims 6 and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Xu (US 20050112544) as applied to claims 5 and 11, and further in view of Sugihara (US 6132683).

With respect to claim 6, Xu discloses the apparatus in claim 5 as set forth in the 35 U.S.C. 102 rejections above, however does not expressly disclose that two reference electrodes are integrated with the insulating layer of the semiconductor substrate.

Sugihara discloses a similar biochip comprising a substrate (Figure 2:2) upon which a cell culture chamber (Figure 2:6) is formed. A plurality of measuring electrodes (Figure 3:11) and conductive traces (Figure 3:12) are located within the cell culture chamber, as well as at least two electrodes (Figure 4:10) acting as a ground reference. This is described in column 6, line 32 to column 7, line 7.

Xu and Sugihara are analogous art because they are from the same field of endeavor regarding biochips comprising microelectrodes configured to evaluate cells.

At the time of the invention, it would have been obvious to ensure that the Xu biochip included at least two electrodes acting as a ground reference. Sugihara teaches in column 1, lines 49-52 that noise is often a problem when measuring very low level or micro-potentials such as cell potentials. Sugihara indicates in column 2, lines 42-52 the use of multiple reference electrodes serves to lower the impedance of the overall system, which thereby lowers the noise often inherent in the measured data.

With respect to claim 15, Xu discloses the apparatus in claim 11 as set forth in the 35 U.S.C. 102 rejections above. As previously described, Xu discloses capacitive metal microelectrodes (Figure 1A:110, 120) positioned on a glass, ceramic and/or silicon substrate in communication with an insulating layer (i.e. silicone-dioxide). Xu, however, does not expressly state that a passivation layer is provided on non-exposed areas between microelectrodes.

Sugihara discloses the apparatus as previously described above. Sugihara additionally indicates in column 7, lines 19-27 that an insulating film (Figure 5:14) is

provided between microelectrodes (Figure 5:11). The insulating film covers areas of the conductive trace (Figure 5:12) that are not exposed by the microelectrodes.

At the time of the invention, it would have been obvious to provide an insulating passivation layer between each of the Xu microelectrodes. Sugihara indicates in column 7, lines 19-27 that it is possible to apply an insulating film in precise locations using known micromachining techniques. One of ordinary skill would have recognized an insulating passivation layer to be beneficial because it would serve to electrically isolate each microelectrode and thereby improve measurement accuracy.

9) Claim 12 is rejected under 35 U.S.C. 103(a) as being unpatentable over Xu (US 20050112544) as applied to claim 11, and further in view of Casnig (US 5134070).

Xu discloses the apparatus in claim 11 as set forth in the 35 U.S.C. 102 rejections above. As noted in the previous rejections above, Xu teaches the use of conductive microelectrodes and traces obtained over a silicon substrate covered with a silicone-dioxide insulating layer. Xu additionally teaches in paragraph [0179] that the electrodes and traces are constructed from metals such as aluminum and gold. Paragraph [0180] indicates that the electrodes and traces are formed by overlaying (i.e. "sandwiching") conductive films that each comprise a different conductive metal. Xu, however, does not disclose the use of titanium nitride as an electrode trace material.

Casnig discloses a cell culture container comprising a substrate (Figure 3:1) coated with a metal distribution electrode (Figure 3:3). Column 7, line 59 to column 8,

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line 49 further teaches that a gold thin film (Figure 4:24) and a titanium nitride coating (Figure 4:2) are additionally provided on the substrate.

Xu and Casnig are analogous art because they are from the same field of endeavor regarding devices for culturing cells on electrode surfaces.

At the time of the invention, it would have been obvious to form the conductive traces of Xu overlaying titanium nitride, aluminum and gold layers. As evidenced by Casnig, titanium nitride is a biocompatible and conductive material well suited for use as an electrode in an apparatus designed to subject a cell culture to an electrical field. Casnig teaches in column 8, lines 31-49 that titanium nitride exhibits desirable qualities relating to chemical/mechanical stability, biological inertness and cost, and is an appropriate material to facilitate cell adhesion.

10) Claims 13 and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Xu (US 20050112544) as applied to claim 11, and further in view of Gomez (US 20030157587).

Xu discloses the apparatus in claim 11 as set forth in the 35 U.S.C. 102 rejections above. As noted in the rejections above, Xu additionally teaches in paragraph [0179] that the electrodes and traces are constructed from metals such as aluminum and gold, and are in communication with metal contact plugs and pads (Figure 1A:150). Xu, however, does not expressly disclose the that microelectrodes are formed using MOS technology.

Gomez discloses a silicon wafer biochip (Figure 1:22) comprising an array of microelectrodes (Figure 1:36) designed to detect an analyte (such as a cell or biomolecule) in solution by measuring impedance. This is set forth in paragraph [0087]. Paragraphs [0147] and [0148] further indicate that the detection electrodes are formed by attaching binding agents to the gate of a silicon MOSFET. MOSFET structures inherently comprise a silicon p-type substrate comprising n-doped regions, a drain, a source and a gate.

Xu and Gomez are analogous art because they are from the same field of endeavor regarding biochip devices comprising microelectrodes configured to measure cell impedance.

At the time of the invention, it would have been obvious to form the electrodes of Xu in communication with MOS transistors. Gomez teaches in paragraphs [0147] and [0148] that MOSFET structures are commonly used in microfluidic biochips with an electrode array to provide an electrical field capable of stimulating and analyzing cells. MOSFET transistors are considered to be very common transistors because they are easily micromachined and highly dependable. Accordingly, one of ordinary skill would have been able to achieve predictable results using MOS technology to construct the microelectrodes of Xu.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to NATHAN A. BOWERS whose telephone number is

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(571) 272-8613. The examiner can normally be reached on Monday-Friday 7 AM to 4 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Marcheschi can be reached on (571) 272-1374. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Nathan A Bowers/
Examiner, Art Unit 1797